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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/575,711	04/13/2006	Hiroyuki Ebinuma	289613US0X PCT	3268

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OBLON, SPIVAK, MCCLELLAND MAIER & NEUSTADT, P.C.
1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER	
DUFFY, PATRICIA ANN	

ART UNIT	PAPER NUMBER
1645	

NOTIFICATION DATE	DELIVERY MODE
06/08/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentdocket@oblon.com
oblonpat@oblon.com
jgardner@oblon.com

Office Action Summary	Application No.	Applicant(s)	
	10/575,711	EBINUMA ET AL.	
	Examiner	Art Unit	
	Patricia A. Duffy	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 March 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-13* is/are pending in the application.

4a) Of the above claim(s) *5-8 and 13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3, 4 and 9-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO AMENDMENT

The amendment filed 3-12-09 has been entered into the record. Claim 2 has been cancelled. Claims 1 and 3-13 are pending. Claims 1, 3, 4 and 9-11 are under examination.

The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

Election/Restrictions

This application contains claims 5-8 and 13 drawn to an invention nonelected with traverse. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Rejections Withdrawn

The rejection of claims 1-4 and 9-12 under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps is withdrawn based on the amendment to the claims.

Rejections Maintained

Claims 1 and 9-10 stand rejected under 35 U.S.C. 102(b) as being anticipated by Waki et al (The Journal of Biological Chemistry, 278(41):40352-40636, 10 October 2003; of record on 1449) for reasons made of record in the Office Action mailed 12-12-08.

Waki et al teach an immunoblot assay wherein a sample containing adiponectin is contacted with a SDS-PAGE 5X sample buffer containing 3% SDS, 50 mM Tris-HCl pH 6.8, 5% 2-mercaptoethanol and 10% glycerol and optionally 10 mM dithiothreitol for complete reduction serum samples (i.e. the instant "at least one of" a reducing agent, an acid or salt thereof and a surfactant). The sample was mixed with 5X sample buffer and incubated for 1 hour at room temperature (see Methods page 40353, column 2 and Results page 40354, column 2). For immunooblotting proteins separated by SDS-PAGE were

transferred to nitrocellulose membranes, the membranes were blocked with TBS-T and then incubated with diluted antiserum for one hour at room temperature (i.e. the instant "use of an insoluble carrier on which an anit-adiponectin antibody is put"). After washing the membranes were incubated with horesradish peroxidase-conjugated anti-rabbit antibody and the binding was detected using ECL western blotting detection. (see page 40353, column 2, third and fourth full paragraph and page 40355, column 1, Figures 2A and 2B and legend). The samples necessarily contained multimer species of adiponectin see Figure 1A page 40354 and Results. Therefore, the serum sample containing multimers of adiponectin were contacted with the 5X buffer containing a detergent and salt of an acid. The sample was allowed to react with the reactant for 1 hour at room temperature. Additionally, medium and cell samples were incubated as with serum subjected to SDS-PAGE, and blotted with anti-globular domain antibodies as described in Figure 6. As such, the method steps have been met. The incubation at room temperature is necessarily a "pre-treatment" to the western blotting immunoassay because it is a treatment before the immunoassay is performed. Therefore, given the claims broadest reasonable interpretation, the method of the art anticipates the claimed method.

Applicant's amendment to claim 1 to remove a reducing agent and in claim 9 to recite the sample is a adiponectin multimer-containing sample does not obviate this issue as the sample buffer contains SDS (a surfactant) and Tris-HCl (a salt of an acid), incubated at 1 hour at room temperature and an immunoassay is subsequently preformed. As such, the art is deemed to anticipate the claims since the reagent is still not seen to require the presence of the protease. In otherwords, the presence of the protease is optional in that not all of the reagents are required in a treatment buffer.

It is noted that the concept of reducing multimers in a sample to a mononmer as discussed in the interview summary is not reflected in the current claims and the specific combination of reagents described in the specification to perform such is not set forth in the claims. Limitations and concepts set forth in the specification are not read into the

claims. The claims do not recite conversion to monomers and immunoassay of the total monomer amount. In fact, the claims require the sample to contain multimers and could read on the assay of multimers since claims and the preamble do not specify this limitation.

Upon reconsideration the art is withdrawn across claims 3, 4, 7 and 8 which require the presence of the protease and subsequent immunoassay.

Claims 1, 3, 4, and 9-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fruebis et al (PNAS 98(4):2005-2010, Feb 13, 2001; of record).

Freubis et al teach immunoassay blotting of Acrp30 (adiponectin) treated with acetylated trypsin that contains the entire globular head region and migrates with an apparent molecular was of 16kDa (Fig 1C, Lane IV). Freubis et al teach that the fragment is more potent than full length protein and that it is presumed that Acrp30 undergoes proteiolysis to generate the C-terminal fragment. Immunoprecipitation studies indicate that plasma has a small mount of the human homolog, apm-1, containing the globular domain of the protein. The source of the trypsin does not structurally distinguish it from that of the prior art (claims 2 and 3). Freubis et al differ by not measuring the amount of gAcrp30 by immunoassay.

It would have been *prima facie* obvious to one having ordinary skill in the art at the time that the invention was made to treat serum/plasma with acetylated trypsin in order to detect the total adiponectin (gAcrp30 + Acrp30) by immunoassay according to Freubis et al because Freubis et al teach that the fragment is more potent than full length protein and that it is presumed that Acrp30 undergoes proteolysis to generate the C-terminal fragment and that the fragment is the active fragment. Pre-treatment conversion of the Acrp30 to gAcrp30 would provide the advantage of having a single homogenous low molecular weight protein to assay.

Appplicants argue that Fruebis et al does not teach treating a sample containing multimers with a reactant. This is not persuasive, Fruebis et al teach that the production of recombinant form of Acrp30 protein that has an apparent molecular mass of 37 kDa and forms a dimer of 74 kDa. The recombinant sample was treatment with the use of acetylated trypsin that "converted" the Acrp30 to a proteolytic fragment that contains the entire head region and migrates with an apparent molecular weight of approximately 16 kDa. As such, the method performed by the art teaches the method steps of the claims (see Results column 2). Applicants argue that Fruebis teaches that trypsin is known to be ineffective of high and medium weight molecular weight multimers of adiponectin. This is not persuasive, the claims do not require conversion to monomers or conversion of the multimers to any specific other form. The specification discusses conversion in a very broad sense as to another form. The conversion of the 37 kDa to the 16 kDa form for analysis meets the claims. The claim merely requires treating a sample containing a multimer with a protease without boiling and as such, the method step of the claim is achieved. The dimer of the art is broadly considered a multimer because a multimer is broadly considered in the art to be two or more monomers. Applicants argue that one skilled in the art would not perform the assay because Pavjani et al (JBC 287(11):9073-9085, 2003) teach that high molecular weight multimers are resistant to trypsin. This is not persuasive because the sample merely comprises a multimer and does not require the high molecular weight multimer to be susceptible to cleavage. Further more Pavjani et al teach that the high molecular weight multimer is most resistant (not totally resistant), the medium molecular weight multimer (hexamer) was more susceptible and the low molecular multimer (trimeric) forms were highly susceptible to proteolysis and the minimal protease resistant core is the globular head domain. One skilled in the art would recognize that certain multimer forms were susceptible to proteolysis. Pavjani et al does not teach that the high and medium multimer forms were totally resistant or trypsin was ineffective in digestion. In fact quite the opposite.. that the hexamer and trimeric forms were

susceptible to trypsin and in all cases the minimal protease resistant core is the globular head domain. The claims do not specify the high molecular weight mutlimer form and as such the claims remain obvious.

Status of Claims

Claims 5-8 and 13 are withdrawn from consideration. Claims 1, 3, 4 and 9-12 stand rejected.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy whose telephone number is 571-272-0855. The examiner can generally be reached on M-Th 7:30 am - 6:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisors, Robert Mondesi can be reached at 571-272-0956.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Patricia A. Duffy/
Primary Examiner